201-15310B

I U C L I D

Data Set

Existing Chemical	:	ID: 3089-11-0
CAS No.	:	3089-11-0
Producer related part		
Company	:	HMMM Coalition
Creation date	:	13.04.2004
Substance related part		
Company	:	HMMM Coalition
Creation date	:	13.04.2004
Status	:	
Memo	:	
Printing date	:	30.04.2004
Revision date	:	13.05.2004
Date of last update	:	14.05.2004
Number of pages	:	53
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	O(CN(c(nc(nc1N(COC)COC)N(COC)COC)n1)COC)C
Molecular formula	:	C15 H30 N6 O6
Molecular weight	:	390.44
Petrol class	:	

29.04.2004

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	liquid
Purity	:	ca. 28 - 52 % w/w
Colour	:	
Odour	:	

Test substance : HMMM cannot be produced commercially in neat (100%) concentration. Instead it is formed as a mixture with methylated melamine formaldehyde polymers. Typical commercial product contains 28-52% HMMM, 47-71% melamine-formaldehyde resin (polymer) (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.

Data obtained by EPIWIN modeling are based on 100% theoretical test substance. For all other data the test substance is described as "other TS," and the concentration of HMMM in the test substance is stated.

29.04.2004

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N'',N''-hexakis(methoxymethyl)-

1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N'',N''-hexakis(methoxymethyl)-

2,4,6-[N,N-Bis(methoxymethyl)amino]-1,3,5-triazine

Hexakis(methoxymethyl)melamin

Hexakis(methoxymethyl)melamine

Hexakis(metoximetil)melamina Hexamethoxy methylmelamine

Hexamethoxymethylmelamine

Hexamethyl methylolmelamine

Hexamethylolmelamine hexamethyl ether

HMMM monomer

Melamine, hexakis(methoxymethyl)-

Melamine, hexakis(methoxymethyl)-

N,N,N',N',N'',N''-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine

Pidifix 330

Triazine [1,3,5]-2,4,6-Triamine, N,N,N',N',N'',N''- hexakis(methoxymethyl)-

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 28 - 33 °C
Sublimation	:	
Method	:	OECD Guideline 102 "Melting Point/Melting Range"
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Result	:	The melting point determination gave a range of 301-306 degrees K +/- 0.5 degrees. Melting began (observance of a very slight meniscus at the top of the white solid mass) at 301 degrees K. At 303 degrees K the test material began to shrink away from the capillary tube wall and became translucent. At 306 degrees K the test material collapsed into a clear liquid.
Test condition	:	The determination was carried out using the capillary method/melting temperature device with liquid bath. A fused capillary tube approximately 80-100 mm long with a 1.0+/- 0.2 mm internal diameter was filled with test material to a level of approximately 3 mm. The filled tube was placed in a freezer overnight to solidify the test substance. The capillary tube was then inserted into the liquid bath such that it touched the middle part of the mercury bulb of the thermometer. The water bath was heated by means of an electric mantle so that the temperature rise was approximately 1 degree C. The bath was stirred constantly with the aid of a magnetic stirrer in the flask. The temperature of the liquid bath was recorded along with any observations relating to the appearance of the test material. The test was performed in duplicate.
Test substance	:	The test substance was CYMEL® 300 Resin (CT-762-02), Batch Number WL6F2361, received by the test laboratory on 17 September 2003. It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.
Reliability	:	(1) valid without restriction OECD Guideline study.
Flag	:	Critical study for SIDS endpoint

22.04.2004 (7)

2.2 BOILING POINT

Value	:	= 448.2 °C at 1013 hPa
Decomposition	:	
Method	:	other
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Test condition	:	Input to model was the CAS No. 3089-11-0. Estimation was by the adapted Stein and Brown method.
Reliability	:	(2) valid with restrictions A reliability rating of 2 has been assigned based on the value being obtained by an approved modeling program.
Flag	:	Critical study for SIDS endpoint

26.04.2004 (12)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .00000014 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated)
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The result was 1.06 x 10-8 mmHg.
Test condition	:	Input to model was the CAS No. 3089-11-0. Estimation was by the Modified Grain method.
Reliability	:	(2) valid with restrictions A reliability rating of 2 has been assigned based on the value being obtained by an approved modeling program.
Flag	:	Critical study for SIDS endpoint

27.04.2004 (12)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 1.61 at 25 °C
pH value	:	= 7
Method	:	other (calculated)
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Test condition	:	Input to model was the CAS No. 3089-11-0.
Reliability	:	(2) valid with restrictions A reliability rating of 2 has been assigned based on the value being obtained by an approved modeling program.
Flag	:	Critical study for SIDS endpoint

26.04.2004 (11)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	water
Value	:	= 69.5 g/l at 20 °C
pH value	:	= 7
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	OECD Guideline 105
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Remark	:	Based on the information obtained in the hydrolysis study carried out on the same test substance by the same laboratory (see Section 3.1.2), it is

evident that some hydrolysis of the sample solution may have occurred during the course of the water solubility test. The overall result was therefore quoted from the sample shaken for the shortest time to minimize any effect the hydrolysis may have had. According to the hydrolysis study the half-life of the test substance in water at pH 7 is 67.0 days, and at pH 4 the half-life is 3.3 hours.

Test condition : The determination was carried out using the flask method, Method 105 of the OECD Guidelines for Testing of Chemicals, July 27, 1995 and Method 830.7840 of the OPPTS Guidelines.

In a preliminary test, an aliquot (1.0037 g) of test material was diluted to 50 ml with glass double-distilled water. After shaking at 30 degrees C for 6 hours and standing at 20 degrees C overnight, the solution was centrifuged at 6,000 rpm for 10 minutes and analyzed. The preliminary estimate of water solubility was 11.2 g/l.

Based on the preliminary result, mixtures of test material and glass double-distilled water were added to three separate flasks. The flasks were shaken at approximately 30 degrees C and after standing at 20 degrees C for a period of at least 24 hours, the contents of the flasks were centrifuged at 6,000 rpm for 10 minutes. The supernatant solution was then sampled using disposable needles and syringes.

The measured pHs of the three test samples were 5.3, 5.8 and 6.0.

The concentration of test material in the sample solutions was determined by high performance liquid chromatography (HPLC). The linearity for the detector response in respect to concentration was assessed over the nominal concentration range of 0 to 200 mg/l. This was satisfactory, with a correlation coefficient of 1,000 being obtained.

Test substance : The test substance was CYMEL® 300 Resin (CT-762-02), Batch Number WL6F2361, received by the test laboratory on 17 September 2003. It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.

Reliability : (1) valid without restriction
OECD Guideline study.

Flag : Critical study for SIDS endpoint
22.04.2004 (7)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	sunlight
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .0000000003235521 cm³/(molecule*sec)
Degradation	:	= 50 % after 23.8 minute(s)
Deg. product	:	not measured
Method	:	other (calculated)
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is relatively rapid.
Test condition	:	Input to model was the CAS No. 3089-11-0.
Reliability	:	(2) valid with restrictions A reliability rating of 2 has been assigned based on the value being obtained by an approved modeling program.
Flag	:	Critical study for SIDS endpoint

27.04.2004 (9)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	= 3.3 hour(s) at 25 °C
t1/2 pH7	:	= 67 day(s) at 25 °C
t1/2 pH9	:	> 1 year at 25 °C
Degradation	:	< 11.3 % after 24 hour(s) at pH 1.2 and 37 °C
Deg. product	:	
Method	:	OECD Guideline 111 "Hydrolysis as a Function of pH"
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Result	:	Graphs of the common logarithm of the concentration (g/l) versus time (hours) were plotted for pH 4 at 30 and 40 degrees C, and pH 7 at 50, 60 and 70 degrees C, and the rate constant and half-life calculated using the standard equations for the method. By plotting the natural logarithm of the rate constants against the reciprocal of the temperature (K), the rate constant and half-lives at 25 degrees C were obtained by extrapolation. The rate constants (s-1) determined were: pH 4: 5.84 pH 7: 1.21 x 10 -7
Test condition	:	The determination was carried out using Method 111 of the OECD Guidelines for Testing of Chemicals, May 12, 1981. The buffer solutions used in the determination were filtered through a 0.2 micron membrane filter to ensure they were sterile before beginning the test. These solutions were also subjected to ultrasonication and degassing

with nitrogen to minimize dissolved oxygen content. The buffer solutions were as follows:

pH 1.2: 50.0 mmol dm-3 potassium chloride and 64.5 mmol dm-3 hydrochloric acid.

pH 4: 12.5 mmol dm-3 potassium hydrogen phthalate.

pH 7: 7.50 mmol dm-3 disodium hydrogen orthophosphate (anhydrous), 5.00 mmol dm-3 potassium dihydrogen orthophosphate, and 5.00 mmol dm-3 sodium chloride.

pH 9: 2.50 mmol dm-3 disodium tetraborate and 5.00 mmol dm-3 sodium chloride.

Sample solutions were prepared in stoppered glass flasks at a nominal concentration of 1.0 g/l in the three buffer solutions. A 1% co-solvent of acetonitrile was used to aid solubility.

A preliminary test was conducted with sample solutions at pH 4, 7, and 9 being maintained at 50.0 +/- 0.5 degrees C for a period of up to 5 days. Results from the preliminary test showed that it was necessary to undertake further testing at pH 4 with solutions maintained at 30.0-40 +/- 0.5 degrees C and at pH 7 with solutions maintained at 50.0, 60.0 and 70.0 +/- 0.5 degrees C. Testing was performed in duplicate at 40 degrees C for pH 4 and 60 degrees C for pH 7. In addition, results from testing at pH 4 showed it was necessary to undertake a further test at pH 1.2, with solutions being maintained at 37.0 +/- 0.5 degrees C for a period of 24 hours.

Aliquots of the sample solutions were taken from the flasks at various times and the pH of each solution recorded.

The concentration of the sample solution was determined in each case by high performance liquid chromatography (HPLC).

Duplicate aliquots of the sample solution were diluted by a factor of 20 using methanol. Duplicate standard solutions of test material were prepared in methanol with relevant buffer solutions.

The linearity of the detector response in respect to concentration was assessed over the nominal concentration range of 0 to 200 mg/l for each standard matrix. This was satisfactory with correlation coefficients of 0.998 to 1.000 being obtained.

Test substance : The test substance was CYMEL® 300 Resin (CT-762-02), Batch Number WL6F2361, received by the test laboratory on 17 September 2003. It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.

Conclusion : The hydrolysis rate increased substantially with lowering pHs, with very little hydrolysis occurring at high pH.

Reliability : (1) valid without restriction
OECD Guideline study.

Flag : Critical study for SIDS endpoint

27.04.2004 (7)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	Fugacity Model Level III
Media	:	
Air	:	.0001 % (Fugacity Model Level I)
Water	:	36.1 % (Fugacity Model Level I)
Soil	:	63.8 % (Fugacity Model Level I)
Biota	:	.0996 % (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other
Year	:	2002
Remark	:	Measured values for melting point and water solubility were obtained on test material that contained about 52% active ingredient. Therefore, these values are not appropriate to input to a program that estimates fugacity of theoretical 100% material.
Result	:	Estimated half-lives are air = 0.7934 hours; water = 3,600 hours, soil = 3,600 hours and sediment = 14,400 hours.
Test condition	:	Input to model was the CAS No. 3089-11-0. Emission rates were assumed to be 1,000 kg/hour for air, water and soil, and 0 kg/hour for sediment.
Reliability	:	(2) valid with restrictions A reliability rating of 2 has been assigned based on the value being obtained by an approved modeling program.
Flag	:	Critical study for SIDS endpoint

27.04.2004 (10)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Contact time	:	29 day(s)
Degradation	:	= 23 (±) % after 28 day(s)
Result	:	other: not readily biodegradable
Kinetic of test subst.	:	3 day(s) = 3 % 10 day(s) = 5 % 16 day(s) = 15 % 22 day(s) = 22 % 29 day(s) = 20 %
Control substance	:	Benzoic acid, sodium salt
Kinetic	:	14 day(s) = 82 % 29 day(s) = 94 %
Deg. product	:	not measured
Method	:	OECD Guideline 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year	:	2004

GLP : yes
Test substance : other TS

Result : The test material attained 23% degradation after 28 days. The increase in organic carbon in both replicate control first absorber vessels, combined with the decrease in inorganic carbon in the first absorber vessel of the second test material replicate on Day 29 resulted in a decrease in the percentage of degradation from Day 28 (23%) to Day 29 (20%).

The test was valid since the total CO2 evolution in the controls on Day 28 was 29.19 mg/l, the IC/TC ratio of the test material at the beginning of the test was < 5%, the difference between the values for CO2 production at the end of the test for the replicate vessels was <20%, the toxicity control attained 51% degradation after 28 days, and sodium benzoate degradation was > = 60% by 14 days. Inorganic carbon analysis of the samples from the second absorber vessels on Day 29 confirmed that no significant carry-over of CO2 into the second absorber vessels occurred.

Observations made throughout the test indicated that the control, test, toxicity and positive control vessels contained light brown dispersions. No undissolved test or positive control material was visible.

Test condition : Test material: The test material (300 mg) was dissolved in culture medium prepared according to the OECD guideline and sonicated for approximately 5 minutes. The volume was adjusted to 1 liter, to give a 300 mg/l stock solution. An aliquot (221 ml) of this stock solution was dispersed in inoculated culture medium and the volume adjusted to 3 liters to give a final concentration of 22.1 mg/l, equivalent to 10 mg carbon/l. The flask containing the test material was inverted several times to ensure homogeneity of the solution.

Standard: An initial stock solution of 1000 mg/l sodium benzoate was prepared by dissolving the standard material directly in culture medium and sonicating the solution for approximately 5 minutes. Additional medium (51.4 ml) was added to the vessel to give a final test concentration of 17.1 mg/l, equivalent to 10 mg carbon/l. The flask containing the test material was inverted several times to ensure homogeneity of the solution.

Toxicity control: An aliquot (221 ml) of the test material stock solution was dispersed in inoculated culture medium alone with an aliquot (51.4 ml) of the sodium benzoate stock solution. The volume was adjusted to 3 liters to give a concentration of 22.1 mg test material/l plus 17.1 mg sodium benzoate/l, equivalent to a total of 20 mg carbon/l.

Bacteria: A mixed population of activated sewage sludge microorganisms was obtained on Nov. 3, 2003 from the aeration stage of the Severn Trent Water Plc sewage treatment plant at Loughborough, Leicestershire, UK, which treats predominantly domestic sewage. The sample was used on the day of collection and maintained under continuous aeration in the laboratory at 21 degrees C. The suspended solids level (3.1 g/l) was determined by filtering a 100 ml sample of the sludge by suction through a pre-weighed GF/A filter paper, drying the paper in an oven (105 degrees C for at least 1 hour), weighing the paper after cooling, and repeating the procedure until a constant weight was obtained.

Test conduct: Approximately 24 hours prior to testing, seven 5 liter glass culture vessels were filled with 2400 ml of culture medium and 29 ml of inoculum (for a total of 30 mg suspended solids/l) and aerated overnight. On Day 0, the test or standard material (for final concentrations of 10 mg carbon/l) were added to duplicate cultures. The test material plus the standard (for a final concentration of 20 mg carbon/l) were added to one vessel to act as a toxicity control. Two vessels left untreated served as inoculum controls. The culture vessels were sealed and CO2-free air was

bubbled through the solution at a rate of approximately 40 ml/min. The CO2-free air was produced by passing compressed air through a glass column containing self-indicating soda lime granules. The solutions were stirred continuously with a magnetic stirrer and maintained in the dark at 21 degrees C.

The CO2 produced was collected in two 500 ml Dreschel bottles containing 350 ml of 0.05 M NaOH. The CO2 absorbing solutions were prepared using purified de-gassed water. Samples (2 ml) were taken from the first CO2 absorber vessel on Days 0, 1, 2, 3, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 27, 28 and 29. The second absorber vessel was sampled on Days 0 and 29. The pH of the solutions was measured on Day 28. After pH was measured, 1 ml of concentrated HCl was added to each vessel to drive off inorganic carbonates. The vessels were resealed, aerated overnight, and sampled on Day 29. All samples (with the exception of samples taken on Days 12 and 18) were analyzed immediately for CO2 (in triplicate) using a TOC analyzer. Samples (300 or 40 microliters) were injected into the inorganic carbon channel of the TOC analyzer. The instrument was calibrated using standard solutions of sodium carbonate. The samples taken on Days 12 and 18 were stored at -20 degrees C and were not analyzed.

On Days 0 and 28, samples (20 ml) were removed from all culture vessels and filtered through 0.45 micron filters prior to DOC analysis. Samples taken on Day 0 were analyzed immediately and those taken on Days 28 were stored at approximately 20 degrees C prior to analysis. The samples (27 or 13 microliters) were injected into the total carbon and inorganic channels of the TOC analyzer in triplicate. The instrument was calibrated using standard solutions of potassium hydrogen phthalate and sodium carbonate.

Calculation of carbon content: The total organic carbon content (TOC) of a 10 mg C/l solution of test material or standard was 30 mg (66.3 mg x 45.2% carbon in the test material and 51.4 mg x 58.34 % carbon in sodium benzoate). The percentage degradation (or the percentage of the theoretical amount of CO2 produced) was calculated by subtracting the amounts of inorganic carbon in the inoculum control from the test (or positive control) samples, dividing the result by the TOC, and multiplying the value by 100%. The percentage degradation from the results of the DOC analysis was calculated by subtracting the DOC values of the inoculum controls from the values of test or positive controls for Days 28 and Days 0, dividing the result on Day 28 by that of Day 0, subtracting it from 1, and multiplying it by 100%. The total CO2 evolution in the control vessels at the end of the test was equal to the mg inorganic carbon in the control x (100 divided by the %C of CO2) x (1/test volume).

Test for validity: The test was considered valid if the degradation of the standard was >= 60% by Day 14, the difference of the extremes of replicated values for CO2 production at the end of the test was < 20%, the total CO2 evolution in the control vessels at the end of the test did not exceed 40 mg/l, and the IC content of the test material at the beginning of the test was < 5% of the TC. The test material was considered to be readily biodegradable if degradation was >= 60% by 28 days. The toxicity control was considered non-inhibitory if degradation was >= 25% by Day 14.

Test substance : The test material was CYMEL® 300 Resin (CT-762-02). It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.

Reliability : (1) valid without restriction
OECD Guideline study.

Flag : Critical study for SIDS endpoint

27.04.2004 (24)

Deg. product	:	
Method	:	other: Estimated by STP Fugacity Model: Predicted Fate in a Wastewater Treatment Facility and by BIOWIN (v.4.000).
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Linear Model Prediction: Does not biodegrade fast Non-linear Model Prediction: Does not biodegrade fast Ultimate Biodegradation Timeframe: Recalcitrant Primary Degradation Timeframe: Weeks-Months MITI Linear Model Prediction: Does not biodegrade fast MITI Non-Linear Model Prediction: Does not biodegrade fast The material is not predicted to be readily biodegradable, but is predicted to be inherently biodegradable.
Reliability	:	(2) valid with restrictions The biodegradation rate was calculated by an accepted method.

15.04.2004 (8)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	>= 603.1
LC50	:	> 603.1
Limit test	:	no
Analytical monitoring	:	no
Method	:	OECD Guideline 203 "Fish, Acute Toxicity Test"
Year	:	1993
GLP	:	yes
Test substance	:	other TS
Remark	:	The LC50 value stated above was based on the Water Accommodated Fraction
Result	:	No mortality occurred during the 96-hour period. No test material insolubility or feces were noted in any replicate chambers. None of the fish exposed to 1,000 mg/l died.
Test condition	:	Fish: This 96-hour static, non-renewal bioassay was performed on six (6) groups of 10 bluegill sunfish approximately 29 weeks of age at initiation of exposure. Fish were maintained at 22.3°C (22.0-22.9) under a 16hr/8hr light/dark cycle. The fish were housed (10 per tank) in 8.5 l glass tanks containing 3.6 l of laboratory dilution water (Blend Water 2). Test water: Water hardness of the dilution water ranged between 72 and 84 mg/l, as CaCO3. Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The pH values were 7.0-7.6. Dissolved oxygen levels ranged from 8.4 (on day 0) - 6.5 (on day 4). The dissolved oxygen values on day 3 dropped below 60% of saturation in some of the chambers. Aeration with glass pipettes was initiated in all test chambers for the remainder of the study. Test concentrations: An initial range finding test was performed to determine the optimal concentrations for the test. The treatment concentrations were: 60, 120, 250, 500, and 1,000 mg/l and a laboratory dilution water control (Blend Water 2). Individual treatments were prepared by adding the appropriate amount of test material to laboratory dilution water which was stirred for 1 hour and 20 minutes until treatment solutions appeared clear. Test conduct: Tests were performed in duplicate. Observations for mortality, abnormal behavior and appearance of the fish were performed on all replicate chambers at 24, 48, 72 and 96 hours. The LC50 was to be determined based on the Water Accommodated Fraction (WAF) of each solution for a period of 96 hours.
Test substance	:	The test material contained 34-44% hexamethoxymethylmelamine (CAS # 3089-11-0) and 38-40% methylated melamine-formaldehyde polymer (CAS # 68002-20-0) .
Reliability	:	(2) valid with restrictions This test was conducted in general agreement with GLP regulations and was performed to comply with OECD GLP regulations.
Flag	:	Critical study for SIDS endpoint.

19.04.2004 (13)

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)

Unit	:	mg/l
NOEC	:	= 320
LC50	:	> 1000
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009
Year	:	1984
GLP	:	yes
Test substance	:	other TS

Result : None of the fish in at any test concentration died by 96 hours. Abnormal effects of surfacing, dark discoloration and/or fish on bottom were observed in the 560 and 1,000 mg/l test concentrations. Therefore, the NOEC and LC50 values in terms of the formulation were 320 mg/l and > 1,000 mg/l, respectively.

The 96-Hr LC50 value for Antimycin A was 1.2 E-4 mg/l.

Test condition : Test water: Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The dissolved oxygen concentrations were adequate (ranged from 7.4 to 9.7 mg/l and represented 84 and 110% saturation at 22 degrees C). The pH values ranged from 7.0 to 7.2. The total hardness of the dilution water was 40-45 mg/l, as CaCO3.

Test concentrations: An initial range finding test was performed to determine the optimal concentrations for the test. The preliminary test concentration was set at 100 mg/l. From this information, five concentrations of the test compound were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/l (100, 180, 320, 560, and 1,000 mg/l) and included a dilution water control and solvent control. The solvent control received an aliquot (7.5 ml) of acetone, equivalent to that used in preparation of all test concentrations. A reference material (Anitmycin A) was used as a challenge to verify that the fish were in good condition.

Test conduct: Ten fish were tested per test condition. The fish were added to the test chambers by random assignment within 30 minutes of addition of test material. The test vessels were kept in a water bath at a constant 22 degrees C. All fish were observed once every 24 hours for mortality and abnormal effects such as surfacing, loss of equilibrium and dark discoloration.

The LC50 value was to be determined from the nominal concentrations of 100, 180, 320, 560, and 1,000 mg/l.

Test substance : The test material contained 28±1% hexamethoxymethylmelamine(CAS # 3089-11-0) and approximately 72% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Meets generally accepted scientific standards and is described in sufficient detail.

19.04.2004 (1)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 560
LC50	:	> 1,000
Limit test	:	no
Analytical monitoring	:	no

Method	:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009
Year	:	1983
GLP	:	yes
Test substance	:	other TS
Result	:	None of the fish in at any test concentration died by 96 hours. Abnormal effects of surfacing and fish on the bottom were observed at 1,000 mg/l. Therefore, the NOEC and LC50 values were 560 mg/l and > 1,000 mg/l, respectively. The 96-Hr LC50 value for Antimycin A was 2.9 E-5 mg/l.
Test condition	:	Test water: Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The dissolved oxygen concentrations were adequate (ranged from 7.6 to 9.5 mg/l and represented 70 and 88% saturation at 12 degrees C). The pH values ranged from 7.0 to 7.6. The total hardness of the dilution water was 40-45 mg/l, as CaCO3. Test concentrations: An initial range finding test was performed to determine the optimal concentrations for the test. The preliminary test concentrations were set at 0.1, 1.0, and 100 mg/l. From this information, five concentrations of the test compound were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/l (100, 180, 320, 560, and 1,000 mg/l) and included a dilution water control and solvent control. The solvent control received an aliquot (7.5 ml) of acetone, equivalent to that used in preparation of all test concentrations. A reference material (Anitmycin A) was used as a challenge to verify that the fish were in good condition. Test conduct: Ten fish were tested per test condition. The fish were added to the test chambers by random assignment within 30 minutes of addition of test material. The test vessels were kept in a water bath at a constant 12 degrees C. All fish were observed once every 24 hours for mortality and abnormal effects such as surfacing, loss of equilibrium and dark discoloration. The LC50 value was to be determined from the nominal concentrations of 100, 180, 320, 560, and 1,000 mg/l.
Test substance	:	The test material contained 28±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 72% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).
Reliability	:	(1) valid without restriction Meets generally accepted scientific standards and is described in sufficient detail

19.04.2004 (2)

Type	:	semistatic
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC50	:	= 680
Method	:	
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Data reported on CITI (Chemical Inspection and Testing Institute) Web site.
Reliability	:	(4) not assignable There is not enough information present to assign a reliability rating.
Type	:	

Species	:	other: Freshwater Fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 673.22 calculated
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: estimated by ECOSAR using triazines as the reference material
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	This estimated value is similar to that obtained experimentally for bluegill sunfish.
Reliability	:	(2) valid with restrictions The LC50 value was calculated by an accepted method.

15.04.2004 (8)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 320
LC50	:	> 1,000
Limit Test	:	no
Analytical monitoring	:	no
Method	:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009
Year	:	1983
GLP	:	yes
Test substance	:	other TS
Result	:	Although no mortality was observed in the test concentrations of 100-1,000 mg/l, abnormal effects of surfacing and daphnids lying on the bottom of the test chambers were observed at the 1,000 and 560 mg/l test concentrations. Therefore, the NOEC and LC50 values were 320 mg/l and > 1,000 mg/l, respectively.
Test condition	:	Test water: The test water was ABC well water with a total hardness of 255 ppm (as CaCO3). Dissolved oxygen concentrations ranged between 8.0 and 8.1 mg/l, representing 87 and 88 percent saturation at 20 degrees C, respectively. The pH values of the treated chambers were consistent with the control and ranged from 8.2 to 8.7. Test concentrations: An initial range finding experiment was conducted using 5 Daphnia each in exposure concentrations of 1.0, 10, and 100 mg/l. From this information, five concentrations were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/l (100, 180, 320, 560 and 1,000 mg/l) and included a control and solvent control. The solvent control received an aliquot of acetone, equivalent to that of the highest test concentration (1.0 ml). Test conduct: The static daphnia bioassay was conducted in 250 ml glass beakers containing 200 ml of test water. Ten Daphnia were tested per condition. The vessels were kept at 20 +/- 2 degrees C in a temperature-controlled area. The lighting was maintained at 50-70 foot candles on a 16 hour daylight photoperiod. All daphnids were observed once every 24 hours for mortality and abnormal effects such as surfacing, clumping, and lying on the bottom of the test chambers.
Test substance	:	The test material contained 28±1% hexamethoxymethylmelamine (CAS #

3089-11-0) and approximately 72% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Meets generally accepted scientific standards and is described in sufficient detail.

Flag : Critical study for SIDS endpoint.

15.04.2004 (3)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 702.2 calculated
Limit Test : no
Analytical monitoring : no
Method : other: estimated by ECOSAR using triazines as the reference material
Year : 2001
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
The LC50 value was calculated by an accepted method.

15.04.2004 (8)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : = 100
EC50 : > 100
Limit test : yes
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2004
GLP : yes
Test substance : other TS

Result : Neither the growth nor the biomass were affected by the presence of 100 mg/l test material. The cell density of control cultures increased by a factor of 68 by 72 hours. No abnormalities were detected in any of the cultures upon microscopic evaluation at 72 hours. All control and test cultures were clear and colorless at the start of the test. At 72 hours, all cultures appeared to be green dispersions. Temperature was maintained at 24 +/- 1 degrees C throughout the test. The pH values of controls increased from pH 7.6 at 0 hours to 8.4 - 8.5 at 72 hours. The pH deviation was within the limits mentioned in the guideline (< 1.5 units). Measured concentrations of test material ranged from 101 to 104% of nominal.

Test condition : Test organisms: The test was carried out using Scenedesmus subspicatus strain CCAP 276/20, obtained from the Culture Collection of Algae and Protozoa (CCAP), Institute of Freshwater Ecology, The Ferry House, Far Sawrey, Ambleside, Cumbria. Cultures were maintained in the laboratory at 21 +/- 1 degrees C under continuous illumination (approx. 7000 lux). The culture medium was prepared using reverse osmosis purified deionized water and the pH adjusted to 7.5 +/- 0.1 with 0.1 N NaOH or HCl. The medium was sterilized by 0.2 micron membrane filtration. Culture medium was periodically replenished. Pre-culture conditions produced an algal suspension of 1.70 x 10E6 cells per ml in log phase growth. The suspension was diluted to a density of 2.18 x 10E4 cells/ml prior to use. At

the start of the test, the culture contained a nominal cell density of 1 x 10E4 cells/ml.

Test material: The test material was heated to approximately 60 degrees C before addition to culture medium to aid dissolution. Test material (100 mg) was dissolved directly in culture medium and the volume adjusted to 500 ml to give a 200 mg/l stock solution. The solutions were inverted several times to ensure adequate mixing and homogeneity. The concentration and stability of the test material in the test medium were verified by chemical analysis at 0 and 72 hours.

Test conduct: Six 250 ml glass, conical flasks containing 100 ml of test solution and three flasks containing control solution (medium only) were prepared. Test solution was prepared by mixing all 500 ml of the 200 mg/l test material stock solution with 500 ml of algal suspension to give the required test concentration of 100 mg/l. This was the maximum concentration mentioned in the guideline and was identified as being suitable in a preliminary range-finding test. The flasks were plugged with polyurethane foam bungs and incubated at 24 +/- 1 degrees C under continuous illumination (approximately 7,000 lux) and constantly shaken at approximately 150 rpm for 72 hours. Samples were taken at 0, 48 and 72 hours and the cell densities determined using a Coulter® Multisizer Particle Counter. Due to a malfunction of the counter at 24 hours, cell densities at this time were determined using a hemocytometer and light microscope. The pH of each flask was determined at the beginning of the test and at 72 hours. The temperature was recorded daily. Water samples were taken from the control (all replicates were pooled) and the 100 mg/l test group (3 replicates were pooled) solutions at 0 and 72 hours for analysis. Duplicate samples were taken and stored at approximately -20 degrees C for further analysis (if necessary).

The area under the curves for the control and test algae were calculated and the percentages of inhibition of growth were compared by comparing the area under the test curve with that of the control curve. The maximum growth rate for each culture was calculated from the straight section of the growth curve. The areas under the growth curves for the test and control algae at 72 hours were compared using a Students t-test incorporating Bartlett's test for homogeneity of variance. All statistical analyses were performed using the SAS computer software package. The critical level of significance was $p < 0.05$.

The test was considered to be valid if the cell concentration of the control cultures increased by a factor of at least 16 after 72 hours.

Test substance : The test material was CYMEL® 300 Resin (CT-762-02). It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water.

Reliability : (1) valid without restriction
OECD Guideline study.

Flag : Critical study for SIDS endpoint.

19.04.2004 (23)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 2,000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: dosed as received
Doses	:	2,000 mg/kg bw
Method	:	other: Limit Test. OPPTS Guideline 870.110/OECD Guideline 401
Year	:	2001
GLP	:	yes
Test substance	:	other TS
Result	:	One out of 5 males and 3/5 females died during the study (for a total of 4/10). All mortality occurred by study day 2. Clinical abnormalities observed during the study included prostration, breathing abnormalities, no feces, apparent hypothermia, dilated pupils, ocular discharge, eyelids partially closed and decreased food consumption. Body weight gain was noted for all surviving animals during the test period. Gross internal observations for the animals that died included foci on the thymus, dark red lungs, blackish-purple spleen, abnormal content of the bladder, and abnormal content of the digestive system. No significant gross internal findings were observed at necropsy on study day 14. The LD50 value is therefore > = 2,000 mg/l.
Test condition	:	The animal room temperature and relative humidity ranges were 18-23ºC and 40-76%, respectively. Room temperature and relative humidity were monitored daily. Food (except during fasting overnight prior to dosing) and water were provided ad libitum. Animals were randomly selected and subjected to a detailed pretest observation prior to dosing. Only healthy animals were chosen for the study. A limit test was performed in which one group of five male and five female rats received a single, oral, 2,000 mg/kg bw dose of the test article. Following dosing, the animals were observed daily for clinical abnormalities and twice daily for health/mortality checks. The animals were weighed before dosing and then weekly. A gross necropsy was performed on all animals at the time of death or scheduled euthanasia (day 14).
Test substance	:	The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).
Reliability	:	(1) valid without restriction OECD Guideline study.
Flag	:	Critical study for SIDS endpoint.

15.04.2004 (25)

Type	:	LD50
Value	:	= 1,600 - 2,000 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	male/female
Number of animals	:	50
Vehicle	:	other: dosed as received

Doses : 625, 1,250, 2,500 or 5,000 mg/kg bw
Method : other: Follows method described in FIFRA (November, 1982 Section 81-1) and in TSCA: Health Effects Test Guidelines, August 1982.
Year : 1984
GLP : no
Test substance : other TS

Remark : A preliminary range-finding study was conducted in which ten (one/sex/dose level) animals received 50, 100, 500, 1,000, or 2,000 mg/kg. No post-mortem examinations were performed. One animal at the 2,000 mg/kg dose level died on study. The doses for the LD50 study were based on this result.

Effects seen in the gastrointestinal tract may represent an irritant effect of the test material on mucosa.

Result : Mortalities were as follows:

Dose Level(mg/kg)	Males	Females	Total	Time to Death
625	0/5	0/5	0/10	-
1,250	1/5	2/5	3/10	22 hrs
2,500	5/5	5/5	10/10	2-47 hrs
5,000	3/5	4/5	7/10	0-47 hrs

The LD50 values calculated from these data were 1,600 mg/kg bw in females 2,000 mg/kg bw in males (for an overall total in males and females of 1,800 mg/kg bw).

Signs seen within 24 hours of dosing in most or all groups included ataxia, hypoactivity, prostration, hypopnea, wet rales and oral, nasal and ocular discharge. Other signs occurred sporadically. Animals which survived beyond 24 hours generally exhibited decreased food consumption and unthrifty coats for several days after dosing. However, all survivors were free of significant abnormalities by termination of the study (day 14).

Examination of animals which died revealed a variety of changes, primarily in the lungs and gastrointestinal tract; most of these were considered to represent postmortem changes or to demonstrate the presence of the test material in the gastrointestinal tract. Reddening of the stomach and intestinal walls and the presence of red fluid in the stomach and intestines were seen in several animals. Animals killed after 14 days exhibited changes similar to those seen in control animals.

Test condition : The animal room temperature and relative humidity ranges were 19.4-24.4ºC and 30-70%, respectively. Room temperature and relative humidity were monitored twice daily. Food (except during fasting overnight prior to dosing) and water were provided ad libitum. Animals were randomly selected and subject to a detailed pretest observation prior to dosing. Only healthy animals were chosen for the study.

Animals were dosed with the test article as received by oral intubation using a ball-tipped intubation needle fitted onto a syringe. Doses (625, 1,250, 2,500 or 5,000 mg/kg bw) were calculated using fasted body weights.

Animals were checked for viability twice daily and were observed for clinical signs at 1, 2, and 4 hours post-dosing and then daily thereafter for 14 days. Body weights were determined pre-fast, just prior to dosing, and on days 7 and 14. Gross postmortem examinations were performed on all animals which died or were found dead during the study. All animals surviving at termination of study on day 14 were killed and examined grossly. All abnormalities were recorded but no tissues were saved.

Test substance : The test material contained approximately 29±1%

hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
The study meets generally accepted scientific standards and is described in sufficient detail.

15.04.2004 (6)

Type : LD50
Value : = 7,400 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: dosed as received
Doses : 5,010, 6,310, 7,940, or 10,000 mg/kg bw
Method : other
Year : 1976
GLP : no
Test substance : other TS

Result : Mortalities were as follows:

Dose Level (mg/kg)	Males	Females	Total	Time to Death
5,010	1/3	0/2	1/5	1-3 days
6,310	0/2	1/3	1/5	
7,940	1/3	2/2	3/5	
10,000	2/2	3/3	5/5	

Clinical signs: Clinical observations included reduced appetite and activity (2 to 4 days in survivors), increasing weakness, collapse, and death.

Gross Postmortem Observations: Gross autopsy showed hemorrhagic areas of the lungs and liver and acute gastrointestinal inflammation. Viscera appeared normal in animals surviving to 14 days.

Test condition : Animals were dosed as received with 5,010, 6,310, 7,940, or 10,000 mg/kg. Animals were observed for signs of toxicity for 14 days. Gross necropsies were performed at termination.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards. Well-documented and acceptable for assessment.

(19)

Type : LD50
Value : = 5,000 - 10,000 mg/kg bw
Species : rat
Strain : other: albino
Sex : male
Number of animals : 10
Vehicle : water
Doses : 5,000 and 10,000 mg/kg bw
Method : other
Year : 1960
GLP : no
Test substance : other TS

Result : Dosages of 5,000 mg/kg bw and 10,000 mg/kg bw produced mortalities of 0/5 and 4/5 during the following seven days. Consequently, the single oral dose LD50 is considered to be greater than 5,000 mg/kg bw (but less than

10,000 mg/kg bw).

Test condition : The material was diluted with water to give a dispersion containing 0.2 g solids per ml and was administered orally (by gavage) to young male albino rats. Animals were observed over a 7-day period for physical condition and mortality.

Test substance : The test material contained 50% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 50% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (4) not assignable
Documentation insufficient for assessment.

15.04.2004 (4)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : > .6 mg/l
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 6
Vehicle : other: dosed as received
Doses : .6 mg/l
Exposure time : 6 hours
Method : other
Year : 1976
GLP : no
Test substance : other TS

Result : None of the animals died during the study. Clinical signs observed in surviving animals during the first day post-exposure consisted of reduced appetite and activity. The fur of the animals was a very slight yellow color upon removal from the chamber. The viscera appeared normal upon gross pathology examination.

Test condition : One group, containing six male rats, was exposed once (whole body) for 6 hours to an atmosphere generated from the test article. The exposure levels were obtained by adjusting the rate at which the test article was supplied to the generator. The initial sample weighed 116.0 g, and the recovered sample was 115.1 g. The nominally calculated vaporized sample was 0.9 g. Temperature (27 degrees C) and relative humidity (80%) in the inhalation chamber were monitored. Airflow was set at 4 l/min. Chamber volume was 35 l.

Clinical signs were observed on the day of exposure and during the 14-day recovery period.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (4) not assignable
Documentation insufficient for assessment.

(18)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 7,940 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female

Number of animals	:	3
Vehicle	:	other: dosed as received
Doses	:	5,010 or 7,940 mg/kg bw
Method	:	other
Year	:	1960
GLP	:	no
Test substance	:	other TS
Result	:	No deaths occurred. Specific signs of toxicity observed included reduced appetite and activity (two to four days). Gross port-mortem examination revealed no significant findings related to treatment.
Test condition	:	A dose of 5,010 or 7,940 mg/kg was administered topically to the skin of 3 rabbits, 1 male at the low dose and 1/sex at the high dose. All animals were throughout the 14-day study. On day 14, surviving animals were euthanized and gross postmortem examinations were performed.
Test substance	:	The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well-documented and acceptable for assessment.

15.04.2004 (15)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	other: dosed as received
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	other: Follows method described in FIFRA (November, 1982 Section 81-1) and in TSCA: Health Effects Test Guidelines, August 1982.
Year	:	1988
GLP	:	yes
Test substance	:	other TS
Result	:	The test material produced generally very mild and transient dermal irritation. One of the six animals was free of dermal irritation. Five animals exhibited very slight (barely perceptible) erythema without edema at 0.5 hours. Some erythema (very slight or slight) was noted at 24 and/or 48 hours; but all animals were free of dermal irritation within 72 hours after application of the test material.
Test condition	:	The animal room temperature and relative humidity ranges were 15.5-21.1ºC and 30-70%, respectively. Room temperature and relative humidity were monitored twice daily. Food and water were provided ad libitum. Light was kept on a 12 hours light, 12 hours dark automatically controlled cycle. Animals were randomly selected and subjected to a pretest observation prior to dosing. Only healthy animals were chosen for the study. The test sites were prepared by closely clipping the hair of each rabbit from the dorsal area of the trunk with an electric clipper, to expose at least 10%

of the body surface area. Twenty four hours after clipping the hair, a single 0.5 ml dose of the test article as received was applied to a 1-inch square gauze patch and applied to each of the 2 test sites (2 intact) on each animal. The patches were held in place with tape and covered with an occlusive binder. The binder was removed 4 hours later, and the test sites were wiped with gauze and acetone to remove remaining test article. Skin reactions were evaluated ~30 minutes after wiping.

Animals were checked for viability twice daily and were observed for clinical signs at 30 minutes and at 24, 48, and 72 hours post-patch removal. At each interval, all sites were evaluated for erythema and edema or other evidence of dermal irritation according to the Draize scoring system (J Pharmacol Exp Therap 82: 377-390, 1944).

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
The study is comparable to a guideline study. It meets generally accepted scientific standards and is described in sufficient detail.

(5)

Species : rabbit
Concentration : undiluted
Exposure :
Exposure time :
Number of animals : 6
Vehicle : other: dosed as received
PDII :
Result : not irritating
Classification :
Method : other: Primary Skin Irritation Study according FHSA
Year : 1976
GLP : no
Test substance : other TS

Result : At the 24-, 48- and 72-hour evaluations, scores for erythema ranged from 1 to 2 for abraded sites and were 0 for intact sites. Scores for edema ranged from 0 for intact sites to a 2 for abraded sites. There were no important differences in skin irritation between intact and abraded sites.

Test condition : A single 0.5 ml dose of the test article was applied to each an intact and abraded site on each animal. Skin reactions were evaluated ~4, 24, hours and at 2, 3, and 7 days.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (4) not assignable
Documentation insufficient for assessment

(17)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 24 hour(s)
Comment :
Number of animals : 6
Vehicle : other: dosed as received
Result : slightly irritating
Classification :

Method	:	other: Primary Eye Irritation Study according to FHSA
Year	:	1976
GLP	:	no
Test substance	:	other TS
Result	:	All rabbits survived. Ocular exposure produced immediate discomfort (considered moderate), with eyes tightly closed. At 10 minutes post exposure there was moderate erythema and copious discharge. At 1 hour there was slight to moderate erythema and copious discharge. At 24 hours there was slight erythema, and copious discharge with slight whitish exudate. By 48 hours there was gradual improvement. By 72 hours there were no signs of irritation. No corneal damage or irisitis was noted at any time in the rabbit's eyes. However, discharge and redness of the conjunctivae were observed in all animals. Irritation to the conjunctivae appeared to dissipate by 48 hours and was not evident by 72 hours. The average of the Draize Irritation Scores for 24, 48 and 72 hours was 8, 1 and 0 on a scale of 110 for the six eyes, respectively.
Test condition	:	A single dose of 100 microliters of undiluted test material was placed in the cupped lower lid of the one of each rabbit; the untreated eye served as the control. The material was left in the eye for 24-hours. During the 7 day study, the eyes were examined for discharge, chemosis, inflammation, and opacity at 10 minutes, 1 hour, 24 hours and on days 2, 3, 5, and 7 after dosing. Ocular Irritation Scores (Draize Scores) were calculated.
Test substance	:	The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).
Reliability	:	(1) valid without restriction Meets generally accepted scientific standards and is described in sufficient detail.

(16)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	28 days (males), 36-52 days (females)
Frequency of treatm.	:	daily
Post exposure period	:	14 day recovery period
Doses	:	250, 500 and 1000 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 250 mg/kg bw
LOAEL	:	= 500 mg/kg bw
Method	:	OECD combined study TG422
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Remark	:	Doses used in this study were based on the results of a preliminary study in which 250, 500 and 1,000 mg/kg/day test material was given by gavage at approximately the same time each day for seven consecutive days. All animals survived to termination. There was no effect of treatment on food

consumption or clinical signs. Slight decreases in mean body weight gain and /or body weight losses were noted in the 1,000 mg/kg/day group during study Days 1 to 3.

The methods and results listed in this summary are for the repeated dose toxicity phase of the OECD 422 study. Methods and results for the reproductive and developmental toxicity phases are listed in their respective sections.

The authors stated that no signs of systemic toxicity were observed at 250 mg/kg/day (although minimal to mild hyperplasia of the limiting ridge of the nonglandular portion of the stomach was observed in males and females at this dose and higher doses). The authors stated that the histopathological effects in the stomach were considered to be gut irritation effects that were not reflective of systemic toxicity.

Result : Overall: All reproductive and recovery phase males survived to scheduled termination. There was no effect of treatment on any FOB or locomotor activity parameter in males or females. Mean absolute and relative left testis weights were increased in all groups of treated males compared to controls. However, the control group testes weights were atypically low, the increases were not dose-dependent, similar changes were not observed in the right testes, and there were no correlating macroscopic or microscopic changes in the testes. Therefore, the changes in left testes weights were not considered to be related to test material.

1,000 mg/kg/day: One reproductive female in this group was euthanized in extremis on gestation day 21. This female was lethargic, prostrate, limp, and had labored respiration and red material around the nose prior to euthanization. Necropsy findings in this female were not remarkable. One female in the recovery phase group was euthanized in extremis on study day 2. Clinical findings in this female were prostration, hypothermia, labored respiration, clear material around the eyes and mouth and increased salivation. This female had white areas on the duodenum and reddened mucosa in the glandular portion of the stomach. Microscopically, this female had lesions in the glandular (neutrophil infiltration, and submucosal edema) and nonglandular (acute inflammation) portions of the stomach. Lymphoid necrosis of the lymphoid organs (thymus, lymph nodes and spleen) and single cell necrosis of the lymphoid cells in the lamina propia of the intestinal tract were also observed. The deaths were considered to be possibly related to treatment.

Three reproductive phase males had prostration, impaired mobility and/or increased salivation after dosing on study days 5 and 6. Increased incidences of lethargy, clear material around the mouth, brown staining around the mouth and/or salivation were noted in reproductive and recovery phase males 1 hour after dosing during study days 1-26. These symptoms were not noted in recovery phase males during the 14 day recovery period. Clinical findings in 1-3 females at the physical examinations and/or 1 hour following dosing included prostration, lethargy, rocking, lurching or swaying while ambulating, red material around the nose, labored respiration and/or splayed forelimbs/hindlimb. Salivation, clear material around the mouth and/or ventral trunk and brown staining around the mouth were found in females in both phases 1 hour after dosing, primarily during the first two weeks of treatment. These findings did not persist into the recovery period.

Mean body weights of reproductive and recovery phase males were decreased during study weeks 0-1, 2-3 and or 3-4. Mean cumulative body weight gain of reproductive males during weeks 0-4 was significantly decreased. Food consumption of males in both phases was decreased during weeks 0-1. Mean absolute and relative (to body weight) adrenal gland weights were increased in reproductive phase males and mean

absolute adrenal gland weights were increased in reproductive phase females. A significant increase in relative (to body weight) thyroid/parathyroid weight was observed in recovery phase males.

Mean red blood cell count, hematocrit, hemoglobin, and reticulocyte counts (absolute and percent) were significantly decreased in reproductive phase males and females. Lymphocyte counts (percent) were also decreased in reproductive phase males. The decrease in the lymphocyte count was considered to be of minimal toxicologic significance because there were no changes in mean white blood cell counts and no correlating changes in lymphoid organs. Platelet counts were increased in reproductive phase females. This was considered to be a spurious result since it was not dose-related and was not observed in males. Mean serum chloride was increased in reproductive phase females. This was no considered to be related to test material since a similar increase was not observed in males and there were no correlating changes in other electrolytes.

Macroscopic lesions were found in the stomach of one reproductive phase male. Correlating microscopic changes (ulceration and submucosal edema of the nonglandular portion of the stomach) were observed in this male. Microscopic changes were observed in reproductive phase males and females in the glandular (minimal neutrophil infiltration, erosion in 1/10 males and 1/10 females and eosinophilic chief cells in 3/10 males and 1/10 females) and nonglandular portion (minimal to mild hyperplasia of the limiting ridge in 9/10 males and 10/10 females) of the stomach. One recovery phase male had minimal hyperplasia of the limiting ridge of the nonglandular portion of the stomach.

500 mg/kg/day: One reproductive phase female died during parturition due to difficult delivery. On the day of death, this female was lethargic, had splayed hindlimbs and red material around the nose, and did not exhibit litter retrieval. At necropsy, this female had foamy contents in the trachea, dark red discoloration of the Harderian glands, mottled lungs that were no fully collapsed and dark red areas of the stomach. Minimal erosion of the glandular mucosa of the stomach was seen in this animal. The death was considered to be possibly related to treatment.

Increased incidences of lethargy, clear material around the mouth, brown staining around the mouth and/or salivation were noted in reproductive phase males 1 hour after dosing during study days 1-26. Salivation, clear material around the mouth and/or ventral trunk and brown staining around the mouth were found in females in both phases 1 hour after dosing, primarily during the first two weeks of treatment. These findings did not persist into the recovery period. Salivation, clear material around the mouth and/or ventral trunk and brown staining around the mouth were found in females in both phases 1 hour after dosing, primarily during the first two weeks of treatment. These findings did not persist into the recovery period.

Hematocrit was decreased and platelet counts were increased in reproductive phase females. The increase in platelet counts was considered to be spurious since it was not dose-dependent and not observed in males. A significant decrease in prothrombin time also was seen in reproductive phase females. This was not considered to be related to treatment since it was not observed in high dose females. Mean serum calcium was increased in reproductive phase females. This was not considered to be related to test material since it did not occur in males and was not dose-related.

Microscopic changes were observed in reproductive phase males and females in the nonglandular portion of the stomach. In the nonglandular portion of the stomach, minimal to mild hyperplasia of the limiting ridge was

observed in 8/10 males and 8/10 females.

250 mg/kg/day: Microscopic changes were observed in reproductive phase males and females in the nonglandular portion of the stomach. In the nonglandular portion of the stomach, minimal to mild hyperplasia of the limiting ridge was observed in 7/10 males and 2/10 females.

Control: One reproductive phase female died on gestation day 8. The cause of death was intubation error.

Test condition : Animals: Sixty one male and 61 sexually mature, virgin female Crl:CD® (SD)IGS BR rats were examined on the day of receipt and weighed the day following receipt. They were approximately 9 weeks old upon arrival. They were observed twice daily for appearance and behavior during a 10 day acclimation period. Body weights, food consumption and clinical condition were recorded for a 1 week pretreatment period.

Animals were individually housed in suspended wire-mesh cages (except during and following mating). Animals were housed in an environmentally-controlled room, under a 12 hour light/dark cycle. The actual mean daily temperature ranging from 71.3 to 71.7 degrees F and a mean daily humidity ranging from 32.7% to 38.5%. Air was changed 10 times per hour. Certified feed and water were supplied ad libitum. No contaminants were present in food and water at levels sufficient to affect the outcome. Feeders were changed and sanitized once per week.

Test material: The appropriate amount of test material for each group was mixed with corn oil to provide for administration of 250, 500 and 1,000 mg/kg bw/day. Each formulation was prepared weekly. The formulations were stirred continuously throughout preparation, sampling and dose administration.

Study design: The animals were randomly allocated by weight to 4 groups of 10 animals per sex (reproductive phase animals) receiving either 0 (vehicle), 250, 500 or 1,000 mg/kg/day test material and two additional groups of 5 animals per sex (recovery phase animals) receiving either 0 (vehicle) or 1,000 mg/kg/day test material. Individual body weights at randomization were within +/- 20% of the mean for each sex. The vehicle (corn oil) and test material suspensions were administered orally by gavage to their respective groups with a 16-gauge dosing cannula once daily at approximately at the same time. The dosing volume was 5 ml/kg. Males used in the reproductive phase and recovery phase males and females received test material for 28 days. Administration for the reproduction phase began 14 days prior to mating and continued through mating. The reproductive phase females received test material for 36-52 days. Five recovery animals per sex in the control and high dose groups were dosed for 28 days, and left untreated for an additional 14 days. The animals were approximately 11 weeks old at the beginning of the study. Weights of males and females to be used in the reproductive phase ranged from 294-386 and 217-264 g, respectively. Weights of males and females to be used in the recovery phase ranged from 340-365 and 222-259 g, respectively. Doses were based on the most recently recorded body weight.

Following 14 days of dosing, 10 reproductive phase males were paired on a 1:1 basis with 10 reproductive phase females from the same group. During mating, the females were paired in the home cage of a male from the same treatment group. Following positive identification of mating (presence of a copulatory plug or the presence of sperm in a vaginal smear following vaginal lavage), the females were individually housed in plastic maternity cages with ground corncob bedding. The day when evidence of mating was identified was termed Day 0 of gestation. The females and their offspring were housed in these cages through lactation day 4 (the

scheduled day of necropsy). Females that did not exhibit evidence of mating after 14 days were separated from males. Additional details about the reproduction and developmental toxicity phases are described under their respective headings.

Parameters evaluated: All animals were observed twice daily for mortality and morbundity. Clinical observations were recorded daily. Animals were observed for toxicity at the time of dosing and approximately 1 hour after dosing. Detailed physical examinations were conducted weekly. Male body weights were recorded weekly, beginning 1 week prior to administration of test material until termination. Body weights of females were recorded weekly, beginning 1 week before dosing and until copulation was observed. After mating, body weights of females were recorded on gestation Days 0, 4, 7, 11, 14, 17 and 20 and on lactation Days 1 and 4. Body weights for recovery phase females were recorded weekly. Body weights of males and females allocated to functional observational battery and locomotor activity assessments also were recorded at the time these tests were performed. Individual food consumption was recorded when body weights were measured except during the breeding period. When food intake could not be measured for one of the days in a given interval (due to a weighing error, food spillage or obvious erroneous value), values were calculated using the appropriate number of days for that interval.

Functional observational battery (FOB) observations were recorded for 5 reproductive phase animals/sex/group. Males were evaluated following approximately 28 days of dose administration. Females were evaluated on lactation day 4 (following 36-52 days of dose administration). The FOB included the following observations: home cage [posture, convulsions/ tremors, feces consistency, biting, palpebral (eyelid) closure], handling (ease of removal from cage, lacrimation/chromodacryorrhea, piloerection, palpebral closure, eye prominence, red/crusty deposits, ease of handling animal in hand, salivation, fur appearance, respiratory rate/character, mucous membranes/eye/skin color, and muscle tone), open field (mobility, rearing, convulsions/tremors, grooming, bizarre stereotypic behavior, time to first step, gait, arousal, urination/defecation, gait score, and backing), sensory (approach, startle, pupil, touch, tail pinch, and eyeblink responses, forelimb and hindlimb extension, air righting reflex and olfactory orientation), neuromuscular [hindlimb extensor strength, hindlimb foot splay, grip strength (hindlimb and forelimb) and rotarod performance], and physiological (catalepsy, body temperature and body weight). Locomotor activity (total, fine and ambulatory activity) was assessed over 60 minutes(12 five minute intervals). Testing was performed blindly, by the same technicians (if possible).

Blood samples for hematology (total and differential leukocyte count, erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count, prothrombin time, activated partial thromboplastin time, and reticulocyte count) and serum chemistry (albumin, total protein, globulin, albumin/globulin ratio, total bilirubin, urea nitrogen, creatinine, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase, glucose, total cholesterol, calcium, chloride, phosphorus, potassium and sodium) evaluations were collected from the vena cavas of five reproductive phase animals/sex per group at necropsy (28 days of dosing for males and lactation day 4 for females). The animals were different from those that were evaluated in the FOB and locomotor activity tests. Blood samples were not taken from females that did not deliver. The animals were not fasted overnight.

A complete necropsy was performed on all animals found dead, or euthanized in extremis or at study termination. All males (both phases) and recovery phase females were euthanized following the completion of

the mating period or at the end of the 14 day recovery period. All reproductive phase females that delivered, failed to deliver or had total litter loss were necropsied on lactation day 4, on post-mating/cohabitation day 25, or within 24 hours of loss, respectively. One female in the 1000 mg/kg/day group with total litter loss was not euthanized within 24 hours of litter loss to ensure that a sufficient number of high dose females were available for FOB, motor activity and clinical pathology evaluations. The necropsy included examination of the external surface, all orifices and the cranial, thoracic, abdominal and pelvic cavities including viscera.
The following organs/tissues were removed and weighed: adrenal glands, brain, epididymides (separately), heart, kidneys, liver, ovaries (with oviducts), spleen, testes (separately), thymus gland and thyroids (with parathyroids). These tissues plus the following tissues and organs were collected and placed in 10% neutral-buffered formalin: aorta, bone (with marrow) bone marrow smear, coagulating gland, eyes (with optic nerve), GI tract, exorbital lacrimal glands, lungs, lymph node (mesenteric and mandibular), mammary gland (females only), pancreas, peripheral nerve (sciatic), pituitary, prostate, salivary gland (mandibular), seminal vesicles, skeletal muscle, skin, spinal cord, trachea, urinary bladder, uterus (with vagina) and all gross lesions. Microscopic examinations were performed on all tissues from controls and high dose reproductive phase animals. The stomachs of all animals in the reproductive phase groups and the high dose recovery animals were examined. Reproductive and developmental toxicity assessments are described in the appropriate sections.

Statistical evaluations: Mean adult (weekly, gestation and lactation) body weight data, food consumption, FOB data, locomotor activity data, clinical pathology, absolute organ weight and relative organ weight (males only) data were subjected to a parametric one-way analysis of variance (ANOVA) to determine intergroup differences. If the ANOVA revealed any significant ($p < 0.05$) variances, Dunnett's test was used to compare group data to control data. FOB parameters that yielded scalar of descriptive data were analyzed using the Fisher's Exact Test. Clinical pathology values for white blood cell types that occurred at low incidences (monocytes, eosinophils and basophils) were not subjected to statistical analysis.

Test substance : The test material was CYMEL® 300 Resin (CT-762-02). It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water. Doses were not adjusted for purity.

Reliability : (1) valid without restriction
OECD Guideline study

Flag : Critical study for SIDS endpoint.

19.04.2004 (26)

Type : sub-acute
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : dermal
Exposure period : 28 days
Frequency of treatm. : five days per week, for approximately four weeks (total exposures were 23 for males and 24 for females)
Post exposure period :
Doses : 250, 750 and 1,000 mg/kg bw/day
Control group : yes
NOAEL : = 1000 mg/kg bw
Method : other
Year : 1990
GLP : yes
Test substance : other TS

Remark : Possible treatment-related effects at either of the two highest doses were increased liver and spleen weights in males, and increased SGOT and SGPT values in females. However, in the absence of supportive microscopic findings, the biological significance of these changes remains unclear. Based on these results, the dose level of 250 mg/kg/day was considered to be the no observable effect level (NOEL) after one month of exposure for rats. The 1,000 mg/kg bw/day dose level was considered to be the no observable adverse effect level.

Result : There were no deaths during the study. Body weights and food consumption of animals at all dose levels were comparable to controls. No clinical signs of dermal irritation or toxicity were observed. There were no significant changes in hematology parameters. Increases in SGOT (mid and high dose females) and SGPT (high dose females) appeared to be related to exposure. Total bilirubin increases in all female exposure groups were attributed to lower than normal control values. Increases in serum globulin and total protein were small in magnitude and did not occur in a dose-related fashion; therefore, they were not considered to be related to treatment.

Gross and Microscopic Pathology: Increases in absolute and relative liver weights (mid and high dose males) and spleen weights (high dose males) may have been related to treatment. Other organ weight alterations were minor and considered to be of no biological significance. There were no treatment-related gross lesions observed at necropsy. A pair of enlarged adrenal glands (control) and a single incidence of hydrometra (an accumulation of watery fluid in the uterus) in two groups (control and low dose) were noted. No microscopic changes were noted in either the control or high dose groups; therefore, the intermediate dose groups were not examined.

Test condition : The test material was applied daily, 5 times per week for approximately 4 weeks, to the shaved upper back (approximately 25 cm2) of groups of ten rats/sex (at 0, 250, 750 and 1,000 mg/kg/day) with a 1cc disposable tuberculin syringe. The total numbers of exposures were 23 for males and 24 for females. The exposure site was not occluded. A plastic collar was placed on the animals for approximately six hours during exposure to minimize ingestion. Skin was then wiped clean of remaining test material after each exposure using ethanol. Daily dosages were calculated form each week's body weight data.

Food and water were available ad libitum. Animals were kept on a 12 hours daily light/12 hours dark cycle. Temperature (64.4 to 78.8 degrees F) and relative humidity (40-70%) were monitored with no excursions. Animals were checked twice daily for mortality and morbidity. Detailed observations for signs of toxicity were made once weekly as were body weight and food consumption measurements.

Clinical pathology was performed at study termination on all animals, with food withheld overnight prior to blood collection. Hematology determinations, leukocyte differentials, reticulocyte counts, and blood chemistry were performed on all animals.

Gross pathology was performed on all animals after week 4. External and internal examinations were performed. The brain, heart, kidneys, liver, spleen, and testes with epididymides (paired organs were weighed together) were weighed.

Histopathology was performed on all control and high dose tissues that were retained. This included the major organs plus the reproductive organs [the ovaries, uterus (corpus and cervix) the mammary glands, the prostate, and the testes with epididymides].

Dunnett's Multiple Comparison Test was used to statistically evaluate

differences between treated and control values for body weights, food consumption and reticulocyte counts. Fisher's Exact Test with Bonferroni's Inequality Procedure was used to evaluate the incidence of microscopic lesions. Other statistical tools were used to evaluate the data depending on whether the data were parametric or non-parametric.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Comparable to a guideline study, conducted under GLP and described in sufficient detail.

15.04.2004 (14)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : S. typhimurium strains TA-98, TA-100, TA-1535, TA-1537 and TA-1538
Test concentration : 167, 500, 1,670, 5,000, 7,500, and 10,000 micrograms/plate (100 microliters test substance/plate)
Cytotoxic concentr. : > 5000 micrograms/plate
Metabolic activation : with and without
Result : negative
Method : other: Standard Ames Protocol
Year : 1988
GLP : yes
Test substance : other TS

Result : Normal growth was observed for all strains at all doses with and without S9. Revertant frequencies for all doses in strains TA1535, TA1537, TA98 and TA100 with and without S9, and in strain TA1538 without S9 approximated those observed in the concurrent negative control cultures. Statistically significant increases in revertant frequencies (to approximately 1.6 times that of control values) were observed in strain TA1538 at doses of 1,670 and 10,000 micrograms/plate in the presence of S9. In addition, the increase was apparently dose-dependent. Therefore, the test material was re-evaluated under identical conditions in strain TA1538 at doses of 167, 500, 1,670, 5,000, 7,500 and 10,000 micrograms/plate with S9. Revertant frequencies for all doses tested in the re-evaluation of strain TA1538 were concurrent with negative control cultures. Thus, the slight increases observed in strain TA1538 with S9 in the original assay are considered to be statistical aberrations due to random fluctuation of the spontaneous revertant frequency. All positive and negative control values in all assays were within acceptable limits.

The results were negative in the Ames/Salmonella Plate Incorporation Assay under the conditions, and according to the criteria, of the test protocol.

Test condition : Test article was prepared by diluting the test material in ethanol. Desired test concentrations were obtained by serial dilution. A preliminary toxicity screen was performed using strains TA-100 and TA-1538 to determine the level of toxicity of the test substance. Five doses, in duplicate, were tested for toxicity with a plate assay performed in the manner used for mutagenicity determinations. Toxicity was assessed at 48 hours after treatment by observing either growth inhibition of the background lawn or a reduction in the number of spontaneous mutants. The maximum concentration tested was 5,000 micrograms/plate. None of the doses were cytotoxic.

Based on these results, 6 concentrations of test material ranging from 167 micrograms/plate to 10,000 micrograms/plate were selected for the

definitive assay. All assays were performed in triplicate cultures in all five tester strains for each test article dose, as well as positive and solvent (ethanol) controls, with and without S9 (50 microliters/plate). S9 was prepared from Aroclor induced rat liver. Positive controls in the absence of S9 were sodium azide (NaN3), 9-aminoacridine (9-AA), and 2-nitrofluorene (2-NF), and the positive control in the presence of S9 was 2-anthramine (2-AA).

Treatments were performed by combining 2 ml top agar (supplemented with 0.5 mM histidine/0.5 mM biotin), 0.1 ml tester strain, 0.1 ml test article (or solvent or positive controls) in sterile glass tubes preheated to 45ºC. The tubes were vortexed and the mixture was poured evenly onto minimal glucose plates, and allowed to solidify. The plates were inverted within an hour and incubated in the dark at 37ºC for 48 hours. Following incubation for 48 hours, the background lawn and spontaneous revertant colonies were enumerated. Inhibited growth was characterized by the absence of a confluent bacterial lawn and /or the presence of pindot colonies.

A positive result was defined as a statistically significant, dose-dependent increase in the number of histidine-independent revertants with at least one dose level inducing a revertant frequency that was two times that of the spontaneous solvent control value. Statistical analyses were performed using the program developed by Snee and Irr (Mutation Res, 85:77-93, 1981), with significance established at the 95% CL. If the test article did not induce a statistically significant, dose-dependent increase in revertant frequency but induced a revertant frequency at one dose level that was two times that of the spontaneous control value, the result was considered equivocal. A negative result was defined as the absence of a statistically significant or dose-dependent increase in the number of histidine-independent revertants.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Comparable to a guideline study, conducted under GLP and is described in sufficient detail.

Flag : Critical study for SIDS endpoint.

(20)

Type : Chromosomal aberration test
System of testing : Chinese Hamster Ovary (CHO) Cells
Test concentration : 87.5, 350 and 900 micrograms/ml without S9 and 292, 1,000 and 2,500 micrograms/ml with S9.
Cytotoxic concentr. : 1,000 to 5,000 micrograms/ml without S9 and 5,000 micrograms/ml with S9.
Metabolic activation : with and without
Result : positive
Method : other
Year : 1989
GLP : yes
Test substance : other TS

Result : Results indicated the test material induced statistically significant increases in aberrations/cell and proportions of cells with aberrant metaphases at 900 micrograms/ml without S9 and at 1,000 and 2,500 micrograms/ml with S9. Addition of S9 mix produced dose-related increases in aberrations/cell and proportions of cells with aberrant metaphases. Therefore, the test material was more clastogenic with exogenous metabolic activation than without.

Test condition : Test materials: The test material was dissolved in 95% ethanol. Doses tested were 87.5, 350 and 900 micrograms/ml without S9 and 292, 1,000 and 2,500 micrograms/ml with S9. The positive control in the absence of S9 was N-methyl-N-nitro-N-nitrosoguanidine (MNNG) dissolved in

ethanol, for a treatment concentration of 2.0 micrograms/ml of medium. The positive control in the presence of S9 was N-Nitrosodimethylamine (DMN) dissolved in distilled water, for a treatment concentration of 1,000 micrograms/ml of medium. The negative (solvent) control with and without metabolic activation was 95% ethanol.

Cytotoxicity: Single cultures of CHO-K1-BH4 cells (Lot #A-12) were prepared at a density of 6 x105 cells/80 cm2 flask in F12FCM(5%) medium containing 5% heat-inactivated fetal bovine serum (FBS). This is a continuous cell line with the modal number of 20 chromosomes and a population doubling time of 12-14 hours. Following the growth period, the medium was aspirated from each flask, the cultures were washed and fresh medium was added. Non-activated cultures were supplied with 10 ml medium and activated cultures with 8 ml medium and 2 ml of S9 mixture isolated from Aroclor- induced rat liver. Treatment was initiated by the addition of 100 microliters of test article (or negative or positive controls) to the appropriate cultures. Cultures were incubated for five hours. After treatment, cultures were washed three times, and medium and BrdUrd were dispensed to each flask. Flasks were incubated for an additional 27 hours. For the last 2-3 hours of incubation, colcemid was added to each culture to arrest cells in metaphase. At the end of incubation, cell suspensions were collected by trypsinization and slides were prepared and stained for sister chromatid differentiation.

Aberration Assay: Duplicate cultures of CHO-K1-BH4 cells were prepared at a density of 8 x 105cells/980 cm2 flask in 15 ml medium containing 5% FBS. Cultures were established for each control and treatment dose level both with and without S9. Cells were allowed to grow for approximately 16-24 hours. Following the growth period, the medium was aspirated from each flask, the cultures were washed, and fresh medium was added. Non-activated cultures were supplied with 10 ml medium and activated cultures with 8 ml medium and 2 ml of S9 mixture. Treatment was initiated by the addition of 100 microliters of test article or control to the appropriate cultures. Cultures were incubated for 5 hours.

Following treatment, cells were washed three times and then fresh medium was added. The cultures were incubated an additional 18 hours. For the last 2-3 hours, colcemid was added to each culture to arrest cells in metaphase.

At the end of incubation, cells suspensions were collected by the mitotic shake-off method. Cells were sedimented by centrifugation and hypotonic KCl was added to swell the cells. Cells were fixed with three washes of methanol:glacial acetic acid (3:1) and slides prepared by standard methods.

A total of 100 metaphases were scored for the presence of chromosome aberrations per data point. Fifty (50) metaphases were obtained per culture and data pooled for analysis. Cytogenetic abnormalities were classified on a standard scoring sheet according to chromosome or chromatid aberrations and further according to type of aberrations. Aberrations were classified according to the nomenclature of Buckton and Evans (Methods for the Analysis of Human Chromosome Aberrations. World Health Organization, Geneva 1973) and Savage (Journal of Med. Genetics 12:103-122, 1975).

Data were evaluated using the Chi-Square analysis. The numbers of aberrant cells in each group were compared to those of concurrent solvent controls.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Comparable to a guideline study, conducted under GLP, and described in sufficient detail.

(21)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	6, 18 and 30 hours
Doses	:	1,700 mg/kg bw
Result	:	negative
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS

Result : Two rats dosed with 1,700 mg/kg died and a few more exhibited severe pharmacotoxic signs. These observations suggest that the test material was evaluated at or near the maximum tolerated dose.

The positive control article, cyclophosphamide, resulted in significant increases in the incidences of chromosome aberrations and in the proportion of metaphases with one or more aberrations.

No statistically significant increase in the incidence of aberrations or in the number of cells with one or more aberrations was observed in animals treated with 1,700 mg/kg at any of the three sampling times evaluated.

The test material was judged to be negative in its ability to induce structural chromosomal aberrations to the hemopoietic cells of the rat bone marrow under the experimental conditions of this assay.

Test condition : A preliminary dose range-finding study (2/sex/group) was performed with doses ranging from 500 – 3,250 mg/kg. Due to the mortality observed at the three highest concentrations of the range finder and the moderate pharmacotoxic signs observed in the next lower dose group (1,500 mg/kg), 1,700 mg/kg was selected as an estimate of the maximum tolerated dose.

The test substance (1,700 mg/kg bw) and the vehicle control (corn oil) were administered in a single oral dose to six groups of male rats and bone marrow cells were harvested at 6, 18 and 30 hours post-dose. Three extra groups (5/sex/group) of rats were also dosed - one with the positive control, cyclophosphamide at 20 mg/kg and the other two groups with the test material at 170 and 935 mg/kg. The three groups were euthanized 18 hours later. Approximately two hours prior to each scheduled termination, animals were administered colchicine at 4 mg/kg bw to arrest cells in metaphase. At the appropriate time, animals were euthanized and both femurs were removed from each animals and metaphase slides prepared. Slides were stained, coded and scored for chromosomal aberrations.

A total of 50 metaphase cells were analyzed for each animal for the presence of chromatid and chromosome type aberrations. Aberrations were classified according to type on a standard scoring sheet and the number of aberrations in each cell tabulated. The numbers of centromeres in each cell were counted and recorded.

Data were evaluated for statistically significant increases in aberrations per

cell in treatment groups as compared to the respective negative control group. The proportion of aberrant metaphases was also evaluated for statistically significant increases over the negative control groups. Data were evaluated separately for each harvest time.

Test substance : The test material contained approximately 29±1% hexamethoxymethylmelamine (CAS # 3089-11-0) and approximately 71% methylated melamine-formaldehyde polymer (CAS # 68002-20-0).

Reliability : (1) valid without restriction
Comparable to a guideline study, conducted under GLP, and described in sufficient detail.

Flag : Critical study for SIDS endpoint.

(22)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : other: combined repeated dose oral toxicity with reproductive/developmental toxicity screening test
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 28 days (males), 36-52 days (females)
Frequency of treatm. : daily
Premating exposure period
Male : 14 days
Female : 14 days
Duration of test : to lactation day 4
No. of generation studies : 1
Doses : 250, 500 and 1,000 mg/kg bw/day
Control group : yes, concurrent vehicle
NOAEL parental : = 250 mg/kg bw
NOAEL F1 offspring : = 500 mg/kg bw
Method : OECD Guideline 422
Year : 2003
GLP : yes
Test substance : other TS

Remark : The NOAEL for systemic toxicity was 250 mg/kg bw/day. The repeated dose toxicity component of this study is discussed in detail in Section 5.4.

Study personnel concluded that there were no signs of systemic, reproductive or developmental toxicity when 250 mg/kg bw/day was administered orally to rats for at least 28 days. However, although possible reproductive toxicity was noted at 500 mg/kg bw/day (one maternal death during parturition), there appeared to be no effect on the F1 fetuses at this concentration. Although the reductions in pup body weights and postnatal survival at 1,000 mg/kg were not statistically significant, study personnel indicated that they were possibly related to treatment. Therefore, the NOAEL for the F1 generation is 500 mg/kg bw/day.

Result : The NOAEL for systemic toxicity was 250 mg/kg bw/day. Systemic effects noted at 500 and 1,000 mg/kg bw/day are described in detail in Section 5.4.

There were no effects of test material on reproductive performance. Male

and female mating indices were 100%, 90%, 100% and 90% in the control, 250, 500 and 1,000 mg/kg bw/day groups, respectively. Male and female fertility indices were 100%, 80%, 100% and 80% in the same groups. Males with evidence of mating that failed to sire a litter were limited to one each in the 250 and 1,000 mg/kg bw/day groups. The mean numbers of days between pairing and coitus in treated F0 females were similar to those of controls.

The mean lengths of gestation in the 250, 500 and 1,000 mg/kg bw/day F0 females (all 22 days) were not significantly different from the study control (22 days) or historical control (21.8 days). One female in the 500 mg/kg group died during parturition (on lactation day 0). This female was lethargic and did not exhibit litter retrieval 1 hour following dosing. Splayed hindlimbs were observed just prior to death. The death was attributed to difficult delivery. This female delivered 3 pups and had 16 fetuses with no apparent malformations retained in utero. One female in the 1,000 mg/kg bw/day group died on gestation day 21 (approaching the time of expected delivery). This female was prostrate and lethargic 1 hour following dosing. This female had 17 fetuses with no apparent malformations and two early resorptions in utero. One control female died of intubation error on gestation day 8. The deaths at 500 and 1,000 mg/kg bw/day were considered to be related to administration of test material.

There were no significant differences between treated animals and controls in the numbers of F1 pups born, live litter sizes and percentages of males at birth. Postnatal survival on postnatal day 0 (relative to number born) and during postnatal intervals 0-1, 1-4 and birth to postnatal day 4 were unaffected by administration of test material. Reductions (not significantly different) in postnatal survival were observed in the 1,000 mg/kg bw/day group during postnatal intervals 0-1 and birth to postnatal day 4. The reduction was due to one female with abnormal nesting behavior (pups not aligned in nest and no litter retrieval) that had a litter of 16 pups that were euthanized in extremis on postnatal day 1. At necropsy, the pups had no milk in their stomachs. No other internal findings were noted in these pups.

The numbers of pups found dead during the lactation period were 2, 2, 1, and 4 in the control, 250, 500 and 1,000 mg/kg bw/day groups, respectively. One pup each in the 500 and 1,000 mg/kg bw/day groups was missing and presumed cannibalized. The pups from one female in the 500 mg/kg bw/day group were euthanized on postnatal day 0 due to death of the dam. The general physical condition of the F1 pups during lactation was generally similar in all groups. Necropsies of all animals found dead, euthanized due to death of the dam, or euthanized at study termination (postnatal day 4) were normal with the following exceptions: one control pup had a major blood vessel variation and one pup in the 1,000 mg/kg bw/day group had anury and tarsal flexure (bilateral).

Mean male and female pup body weights in the 1,000 mg/kg bw/day group were slightly reduced (9.0 - 9.9%, not statistically significant) during postnatal day 1-4. On postnatal day 1, the mean body weight for the 1,000 mg/kg bw/day males (6.4 g) was below the minimum value for historical controls (6.5 g).

Test condition : Animals: Sixty one male and 61 sexually mature, virgin female Crl:CD® (SD)IGS BR rats were examined on the day of receipt and weighed the day following receipt. They were approximately 9 weeks old upon arrival. They were observed twice daily for appearance and behavior during a 10 day acclimation period. Body weights, food consumption and clinical condition were recorded for a 1 week pretreatment period.

Animals were individually housed in suspended wire-mesh cages (except during and following mating). Animals were housed in an environmentally-controlled room, under a 12 hour light/dark cycle. The actual mean daily

temperature ranging from 71.3 to 71.7 degrees F and a mean daily humidity ranging from 32.7% to 38.5%. Air was changed 10 times per hour. Certified feed and water were supplied ad libitum. No contaminants were present in food and water at levels sufficient to affect the outcome. Feeders were changed and sanitized once per week.

Test material: The appropriate amount of test material for each group was mixed with corn oil to provide for administration of 250, 500 and 1,000 mg/kg bw/day. Each formulation was prepared weekly. The formulations were stirred continuously throughout preparation, sampling and dose administration.

Study design: The animals were randomly allocated by weight to 4 groups of 10 animals per sex (F0 animals) receiving either 0 (vehicle), 250, 500 or 1,000 mg/kg/day test material and two additional groups of 5 animals per sex (recovery phase animals) receiving either 0 (vehicle) or 1,000 mg/kg/day test material. Procedures involving recovery phase animals are discussed in Section 5.4. Individual body weights at randomization were within +/- 20% of the mean for each sex. The vehicle (corn oil) and test material suspensions were administered orally by gavage to their respective groups with a 16-gauge dosing cannula once daily at approximately at the same time. The dosing volume was 5 ml/kg. F0 Males received test material for 28 days. Administration to F0 males and females began 14 days prior to mating and continued through mating. The F0 females received test material for 36-52 days. The animals were approximately 11 weeks old at the beginning of the study. Weights of F0 males and females ranged from 294-386 and 217-264 g, respectively. Doses were based on the most recently recorded body weight.

Following 14 days of dosing, 10 F0 males were randomly paired on a 1:1 basis with 10 F0 females from the same group. At the time of mating, male body weights ranged from 341 g to 441 g and female body weights ranged from 221 to 284 g. The animals were approximately 12 weeks old. During mating, the females were paired in the home cage of a male from the same treatment group. Following positive identification of mating (presence of a copulatory plug or the presence of sperm in a vaginal smear following vaginal lavage), the females were individually housed in plastic maternity cages with ground corncob bedding. The day when evidence of mating was identified was termed Day 0 of gestation. The females and their offspring were housed in these cages through lactation day 4 (the scheduled day of necropsy). Females that did not exhibit evidence of mating after 14 days were separated from males. The F0 generation was mated once to allow production of one litter per dam (the F1 litters). Pre-coital intervals were calculated according to the following method: rats paired over a 12-hour dark cycle were considered to have been paired for 1 day. The mating and fertility indices were calculated. Following mating, all F0 females were allowed to deliver naturally and rear their young to postnatal day 4. During the period of expected parturition, the females were observed twice daily for parturition and signs of dystocia. On the day parturition was complete, pups were sexed and examined for gross malformations. The numbers of stillborn and live pups were recorded. Individual gestation lengths were calculated using the date delivery started.

All F0 animals were observed twice daily for mortality and morbundity. Clinical observations were recorded daily. Animals were observed for toxicity at the time of dosing and approximately 1 hour after dosing. Detailed physical examinations were conducted weekly. Male body weights were recorded weekly, beginning 1 week prior to administration of test material until termination. Body weights of females were recorded weekly, beginning 1 week before dosing and until copulation was observed. After mating, body weights of females were recorded on gestation Days 0, 4, 7, 11, 14, 17 and 20 and on lactation Days 1 and 4. Body weights of F0

males and females allocated to functional observational battery and locomotor activity assessments also were recorded at the time these tests were performed. Individual food consumption was recorded when body weights were measured except during the breeding period. When food intake could not be measured for one of the days in a given interval (due to a weighing error, food spillage or obvious erroneous value), values were calculated using the appropriate number of days for that interval.

Functional observational battery (FOB) and locomotor activity observations were recorded for 5 F0 animals/sex/group. Males were evaluated following approximately 28 days of dose administration. Females were evaluated on lactation day 4 (following 36-52 days of dose administration). The tests are described in greater detail in Section 5.4

Blood samples for hematology and serum chemistry evaluations were collected from the vena cavas of five F0 animals/sex per group at necropsy (28 days of dosing for males and lactation day 4 for females). The indices measured are described in greater detail in Section 5.4. The animals were different from those that were evaluated in the FOB and locomotor activity tests. Blood samples were not taken from females that did not deliver. The animals were not fasted overnight.

A complete necropsy was performed on all F0 animals found dead, or euthanized in extremis or at study termination. All males were euthanized following the completion of the mating period. All F0 females that delivered, failed to deliver or had total litter loss were necropsied on lactation day 4, on post-mating/cohabitation day 25, or within 24 hours of loss, respectively. One female in the 1,000 mg/kg/day group with total litter loss was not euthanized within 24 hours of litter loss to ensure that a sufficient number of high dose females were available for FOB, motor activity and clinical pathology evaluations. The necropsy included examination of the external surface, all orifices and the cranial, thoracic, abdominal and pelvic cavities including viscera. Organs that were weighed and examined microscopically are listed in Section 5.4.

Each litter was examined twice daily for survival, and all deaths were recorded. Each pup was weighed, sexed and examined on postnatal days 1 and 4. Any abnormalities in nesting and nursing behavior were recorded. A daily record of litter size was maintained. All surviving pups were euthanized and necropsied on postnatal day 4, with an emphasis placed on developmental morphology. Intact offspring that died or were euthanized in extremis were necropsied. Organs and/or tissues were preserved in 10% neutral-buffered formalin for possible future histopathologic examination.

Statistical evaluations: Parental mating and fertility indices were analyzed using the Chi-square test with Yates' correction factor. Mean adult (weekly, gestation and lactation) and offspring body weight data, adult food consumption, pre-coital intervals, gestation lengths, implantation sites, live litter sizes, unaccounted sites, numbers of pups born and other data described in Section 5.4 were subjected to a parametric one-way analysis of variance (ANOVA) to determine intergroup differences. If the ANOVA revealed any significant ($p < 0.05$) variances, Dunnett's test was used to compare test group data to control data. Mean litter proportions (percent per litter) of postnatal pup survival and pup sexes at birth (percentage of males per litter) were analyzed using the Kruskal-Wallis nonparametric ANOVA test to uncover intergroup differences. If the ANOVA revealed any significant ($p < 0.05$) variances, the Mann-Whitney U-test was used to compare test group data to control data.

Test substance : The test material was CYMEL® 300 Resin (CT-762-02). It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water. Doses were not adjusted for purity.

Reliability	:	(1) valid without restriction OECD Guideline study
Flag	:	Critical study for SIDS endpoint.

19.04.2004 (26)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	28 days (males), 36-52 days (females)
Frequency of treatm.	:	daily
Duration of test	:	to lactation day 4
Doses	:	250, 500 and 1,000 mg/kg bw/day
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 250 mg/kg bw
NOAEL teratogen.	:	= 1,000 mg/kg bw
NOAEL Fetotoxicity	:	= 500 mg/kg bw
Result	:	not developmentally toxic at nonmaternally toxic doses
Method	:	other: OECD Guideline 422
Year	:	2003
GLP	:	yes
Test substance	:	other TS

Remark : The NOAEL for systemic toxicity was 250 mg/kg bw/day. The repeated dose toxicity component of this study is discussed in detail in Section 5.4.

Study personnel concluded that there were no signs of systemic, reproductive or developmental toxicity when 250 mg/kg bw/day was administered orally to rats for at least 28 days. However, although possible reproductive toxicity was noted at 500 mg/kg bw/day (one maternal death during parturition), there appeared to be no effect on the F1 fetuses at this concentration. Although the reductions in pup body weights and postnatal survival at 1,000 mg/kg were not statistically significant, study personnel indicated that they were possibly related to treatment. Therefore, the NOAEL for fetotoxicity is 500 mg/kg bw/day. The authors did not mention whether the malformation in one pup in the 1,000 mg/kg bw/day was thought to be related to administration of test material. Because of the low incidence, the summary preparer considers it to be unrelated to test material. Therefore, the NOAEL for teratogenicity is 1,000 mg/kg bw/day.

Result : The NOAEL for systemic toxicity was 250 mg/kg bw/day. Systemic effects noted at 500 and 1,000 mg/kg bw/day are described in detail in Section 5.4.

There were no effects of test material on reproductive performance. Male and female mating indices were 100%, 90%, 100% and 90% in the control, 250, 500 and 1000 mg/kg bw/day groups, respectively. Male and female fertility indices were 100%, 80%, 100% and 80% in the same groups. Males with evidence of mating that failed to sire a litter were limited to one each in the 250 and 1,000 mg/kg bw/day groups. The mean numbers of days between pairing and coitus in treated F0 females were similar to those of controls.

The mean lengths of gestation in the 250, 5000 and 1,000 mg/kg bw/day F0 females (all 22 days) were not significantly different from the study control (22 days) or historical control (21.8 days). One female in the 500 mg/kg group died during parturition (on lactation day 0). This female was lethargic and did not exhibit litter retrieval 1 hour following dosing. Splayed

hindlimbs were observed just prior to death. The death was attributed to difficult delivery. This female delivered 3 pups and had 16 fetuses with no apparent malformations retained in utero. One female in the 1,000 mg/kg bw/day group died on gestation day 21 (approaching the time of expected delivery). This female was prostrate and lethargic 1 hour following dosing. This female had 17 fetuses with no apparent malformations and two early resorptions in utero. One control female died of intubation error on gestation day 8. The deaths at 500 and 1,000 mg/kg bw/day were considered to be related to administration of test material.

There were no significant differences between treated animals and controls in the numbers of F1 pups born, live litter sizes and percentages of males at birth. Postnatal survival on postnatal day 0 (relative to number born) and during postnatal intervals 0-1, 1-4 and birth to postnatal day 4 were unaffected by administration of test material. Reductions (not significantly different) in postnatal survival were observed in the 1,000 mg/kg bw/day group during postnatal intervals 0-1 and birth to postnatal day 4. The reduction was due to one female with abnormal nesting behavior (pups not aligned in nest and no litter retrieval) that had a litter of 16 pups that were euthanized in extremis on postnatal day 1. At necropsy, the pups had no milk in their stomachs. No other internal findings were noted in these pups.

The numbers of pups found dead during the lactation period were 2, 2, 1, and 4 in the control, 250, 500 and 1,000 mg/kg bw/day groups, respectively. One pup each in the 500 and 1,000 mg/kg bw/day groups was missing and presumed cannibalized. The pups from one female in the 500 mg/kg bw/day group were euthanized on postnatal day 0 due to death of the dam. The general physical condition of the F1 pups during lactation was generally similar in all groups. Necropsies of all animals found dead, euthanized due to death of the dam, or euthanized at study termination (postnatal day 4) were normal with the following exceptions: one control pup had a major blood vessel variation and one pup in the 1,000 mg/kg bw/day group had anury and tarsal flexure (bilateral).

Mean male and female pup body weights in the 1,000 mg/kg bw/day group were slightly reduced (9.0 - 9.9%, not statistically significant) during postnatal day 1-4. On postnatal day 1, the mean body weight for the 1000 mg/kg bw/day males (6.4 g) was below the minimum value for historical controls (6.5 g).

Test condition : Animals: Sixty one male and 61 sexually mature, virgin female Crl:CD® (SD)IGS BR rats were examined on the day of receipt and weighed the day following receipt. They were approximately 9 weeks old upon arrival. They were observed twice daily for appearance and behavior during a 10 day acclimation period. Body weights, food consumption and clinical condition were recorded for a 1 week pretreatment period.

Animals were individually housed in suspended wire-mesh cages (except during and following mating). Animals were housed in an environmentally-controlled room, under a 12 hour light/dark cycle. The actual mean daily temperature ranging from 71.3 to 71.7 degrees F and a mean daily humidity ranging from 32.7% to 38.5%. Air was changed 10 times per hour. Certified feed and water were supplied ad libitum. No contaminants were present in food and water at levels sufficient to affect the outcome. Feeders were changed and sanitized once per week.

Test material: The appropriate amount of test material for each group was mixed with corn oil to provide for administration of 250, 500 and 1,000 mg/kg bw/day. Each formulation was prepared weekly. The formulations were stirred continuously throughout preparation, sampling and dose administration.

Study design: The animals were randomly allocated by weight to 4 groups

of 10 animals per sex (F0 animals) receiving either 0 (vehicle), 250, 500 or 1,000 mg/kg/day test material and two additional groups of 5 animals per sex (recovery phase animals) receiving either 0 (vehicle) or 1,000 mg/kg/day test material. Procedures involving recovery phase animals are discussed in Section 5.4. Individual body weights at randomization were within +/- 20% of the mean for each sex. The vehicle (corn oil) and test material suspensions were administered orally by gavage to their respective groups with a 16-gauge dosing cannula once daily at approximately at the same time. The dosing volume was 5 ml/kg. F0 Males received test material for 28 days. Administration to F0 males and females began 14 days prior to mating and continued through mating. The F0 females received test material for 36-52 days. The animals were approximately 11 weeks old at the beginning of the study. Weights of F0 males and females ranged from 294-386 and 217-264 g, respectively. Doses were based on the most recently recorded body weight.

Following 14 days of dosing, 10 F0 males were randomly paired on a 1:1 basis with 10 F0 females from the same group. At the time of mating, male body weights ranged from 341 g to 441 g and female body weights ranged from 221 to 284 g. The animals were approximately 12 weeks old. During mating, the females were paired in the home cage of a male from the same treatment group. Following positive identification of mating (presence of a copulatory plug or the presence of sperm in a vaginal smear following vaginal lavage), the females were individually housed in plastic maternity cages with ground corncob bedding. The day when evidence of mating was identified was termed Day 0 of gestation. The females and their offspring were housed in these cages through lactation day 4 (the scheduled day of necropsy). Females that did not exhibit evidence of mating after 14 days were separated from males. The F0 generation was mated once to allow production of one litter per dam (the F1 litters). Pre-coital intervals were calculated according to the following method: rats paired over a 12-hour dark cycle were considered to have been paired for 1 day. The mating and fertility indices were calculated. Following mating, all F0 females were allowed to deliver naturally and rear their young to postnatal day 4. During the period of expected parturition, the females were observed twice daily for parturition and signs of dystocia. On the day parturition was complete, pups were sexed and examined for gross malformations. The numbers of stillborn and live pups were recorded. Individual gestation lengths were calculated using the date delivery started.

All F0 animals were observed twice daily for mortality and morbundity. Clinical observations were recorded daily. Animals were observed for toxicity at the time of dosing and approximately 1 hour after dosing. Detailed physical examinations were conducted weekly. Male body weights were recorded weekly, beginning 1 week prior to administration of test material until termination. Body weights of females were recorded weekly, beginning 1 week before dosing and until copulation was observed. After mating, body weights of females were recorded on gestation Days 0, 4, 7, 11, 14, 17 and 20 and on lactation Days 1 and 4. Body weights of F0 males and females allocated to functional observational battery and locomotor activity assessments also were recorded at the time these tests were performed. Individual food consumption was recorded when body weights were measured except during the breeding period. When food intake could not be measured for one of the days in a given interval (due to a weighing error, food spillage or obvious erroneous value), values were calculated using the appropriate number of days for that interval.

Functional observational battery (FOB) and locomotor activity observations were recorded for 5 F0 animals/sex/group. Males were evaluated following approximately 28 days of dose administration. Females were evaluated on lactation day 4 (following 36-52 days of dose administration). The tests are described in greater detail in Section 5.4

Blood samples for hematology and serum chemistry evaluations were collected from the vena cavas of five F0 animals/sex per group at necropsy (28 days of dosing for males and lactation day 4 for females). The indices measured are described in greater detail in Section 5.4. The animals were different from those that were evaluated in the FOB and locomotor activity tests. Blood samples were not taken from females that did not deliver. The animals were not fasted overnight.

A complete necropsy was performed on all F0 animals found dead, or euthanized in extremis or at study termination. All males were euthanized following the completion of the mating period. All F0 females that delivered, failed to deliver or had total litter loss were necropsied on lactation day 4, on post-mating/cohabitation day 25, or within 24 hours of loss, respectively. One female in the 1,000 mg/kg/day group with total litter loss was not euthanized within 24 hours of litter loss to ensure that a sufficient number of high dose females were available for FOB, motor activity and clinical pathology evaluations. The necropsy included examination of the external surface, all orifices and the cranial, thoracic, abdominal and pelvic cavities including viscera. Organs that were weighed and examined microscopically are listed in Section 5.4.

Each litter was examined twice daily for survival, and all deaths were recorded. Each pup was weighed, sexed and examined on postnatal days 1 and 4. Any abnormalities in nesting and nursing behavior were recorded. A daily record of litter size was maintained. All surviving pups were euthanized and necropsied on postnatal day 4, with an emphasis placed on developmental morphology. Intact offspring that died or were euthanized in extremis were necropsied. Organs and/or tissues were preserved in 10% neutral-buffered formalin for possible future histopathologic examination.

Statistical evaluations: Parental mating and fertility indices were analyzed using the Chi-square test with Yates' correction factor. Mean adult (weekly, gestation and lactation) and offspring body weight data, adult food consumption, pre-coital intervals, gestation lengths, implantation sites, live litter sizes, unaccounted sites, numbers of pups born and other data described in Section 5.4 were subjected to a parametric one-way analysis of variance (ANOVA) to determine intergroup differences. If the ANOVA revealed any significant ($p < 0.05$) variances, Dunnett's test was used to compare test group data to control data. Mean litter proportions (percent per litter) of postnatal pup survival and pup sexes at birth (percentage of males per litter) were analyzed using the Kruskal-Wallis nonparametric ANOVA test to uncover intergroup differences. If the ANOVA revealed any significant ($p < 0.05$) variances, the Mann-Whitney U-test was used to compare test group data to control data.

Test substance : The test material was CYMEL® 300 Resin (CT-762-02). It contained 52% CAS No. 3089-11-0, 47% melamine-formaldehyde resin (CAS No. 68002-20-0), < 1% methanol (CAS No. 7732-18-5), 0.15% formaldehyde (CAS No. 50-00-0) and 0.09% water. Doses were not adjusted for purity.

Reliability : (1) valid without restriction
OECD Guideline study

19.04.2004 (26)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) ABC Laboratories, Inc. Columbia, MO. Acute Toxicity of Resimene® 745 to Bluegill Sunfish, Report # 31224. Conducted for Monsanto Company, January 27, 1984 (unpublished study).

(2) ABC Laboratories, Inc. Columbia, MO. Acute Toxicity of Resimene® 745 to Rainbow Trout, Report # 31225. Conducted for Monsanto Company, December 22, 1983 (unpublished study).

(3) ABC Laboratories, Inc., Columbia, Missouri. Acute Toxicity of Resimene® 745 to Daphnia magna; Final Report # 31226 (unpublished study).

(4) American Cyanamid, Acute Oral Toxicity, December, 1960 (unpublished study).

(5) Bio/Dynamics for Monsanto Company. Primary Dermal Irritation Study. Report #4398-87/BD-87-190, January, 1988 (unpublished study).

(6) Bio/Dynamics Inc for Monsanto Company. Acute Oral Toxicity Study in Rats. Report # 4702-83/BD-83-268, August, 1984 (unpublished study).

(7) Cuthbert JE and Mullee DM, Determination of General Physico-Chemical Properties of Cymel® 300 Resin (CT-762-02), SafePharm Laboratories Project Number 971/231, dated November 26, 2003 (unpublished study).

(8) EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000.

(9) EPIWIN AOP (v1.90) model program.

(10) EPIWIN Fugacity Level III Model Program.

(11) EPIWIN KowWin (v1.66) model program.

(12) EPIWIN Mpbpwin (v1.40) model program.

(13) Exxon Biomedical Sciences, Inc. Project Number: 142940, Fish, Acute Toxicity Test, Conducted for Cytec Industries Inc., May 7, 1993 (unpublished study).

(14) Monsanto Agricultural Company, Environmental Health Laboratory. One Month Dermal Study of Resimene® 745 Methylated Melamine-Formaldehyde Resin in Sprague-Dawley Rats. Report # MSL-10185, May 30, 1990 (unpublished study).

(15) Monsanto Company, Acute Dermal Toxicity, August, 1976 (unpublished study).

(16) Monsanto Company, Primary Eye Irritation, August, 1976 (unpublished study).

(17) Monsanto Company, Primary Skin Irritation, August, 1976 (unpublished study).

(18) Monsanto Company. Acute Inhalation Toxicity, August, 1976 (unpublished study).

(19) Monsanto Company. Acute Oral Toxicity, August, 1976 (unpublished study).

(20) Pharmakon Research International for Monsanto Company, Ames/Salmonella Plate Incorporation Assay PH 301-MO-003-88 (PK-88-402) of Resimene® 745 Lot#8951078, December 10, 1988 (unpublished study).

(21) Pharmakon Research International for Monsanto Company, In Vitro Chromosome Aberration Analysis In Chinese Hamster Ovary (CHO) Cells PH 320-MO-004-88 (PK-88-403) of Resimene® 745, February 15, 1989 (unpublished study).

(22) Pharmakon Research International for Monsanto Company, In Vivo Bone Marrow Cytogenetics Rat Metaphase Analysis. PH 315-MO-001-89 (PK-89-74) of Resimene® 745, April 10, 1989 (unpublished study).

(23) Safepharm Laboratories Limited. Cymel® 300 Resin (CT-762-02): Algal inhibition test. SPL Project Number: 971/232, dated Mar 2, 2004.

(24) Safepharm Laboratories Limited. Cymel® 300 Resin (CT-762-02): Assessment of ready biodegradability; CO2 evolution test. SPL Project Number: 971/233, dated Jan 28, 2004 (unpublished study).

(25) Springborn Laboratories, Inc. An Acute Oral Toxicity Study in Rats with Resimene® 745. Study Report #3463.98/SB200110015, for Solutia, Inc. November 12, 2001

(26) WIL Research Laboratories, Inc. A combined 28-day repeated dose oral toxicity with the reproduction/developmental toxicity screening test of CT-762-02 in rats, with a two-week recovery. Study Number WIL-468002, dated September 4, 2003.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT